

WE CLAIM

1. A substantially purified protein, having serine protease inhibitory activity, selected from the group of proteins consisting of materials each of which comprises one of the following amino acid sequences, the amino acids of said sequences being numbered in accordance with the amino acid sequence of native human placental bikunin shown in figure 4F in which the N-terminal residue generated by removal of signal peptide is designated as residue 1:

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ADRERSIHDF CLVSKVVGRC RASMPRWYV VTDGSCQLFV YGGCDGNSNN 50
YLTKEECLKK CATVTENATG DLATSRNAAD SSVPSAPRRQ DSEDHSSDMF 100
NYEEYCTANA VTGPCRASFP RWYFDVERNS CNNFIYGGCR GNKNSYRSEE 150
ACMLRCFRQQ ENPPLPLGSK

(SEQ ID NO.:52);

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MAQLCGL RRSRAFLALL GSLLLGVLA -1
ADRERSIHDF CLVSKVVGRC RASMPRWYV VTDGSCQLFV YGGCDGNSNN 50
YLTKEECLKK CATVTENATG DLATSRNAAD SSVPSAPRRQ DSEDHSSDMF 100
NYEEYCTANA VTGPCRASFP RWYFDVERNS CNNFIYGGCR GNKNSYRSEE 150
ACMLRCFRQQ ENPPLPLGSK VVVLAGLFVM VLILFLGASM VYLIRVARRN 200
QERALRTVWS SGDDKEQLVK NTYVL 225
(SEQ ID NO.: 49).

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25 ADRERSIHDF CLVSKVVGRC RASMPRWYV VTDGSCQLFV YGGCDGNSNN 50
YLTKEECLKK CATVTENATG DLATSRNAAD SSVPSAPRRQ DSEDHSSDMF 100
NYEEYCTANA VTGPCRASFP RWYFDVERNS CNNFIYGGCR GNKNSYRSEE 150
ACMLRCFRQQ ENPPLPLGSK VVVLAGLFVM VLILFLGASM VYLIRVARRN 200
QERALRTVWS SGDDKEQLVK NTYVL 225

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(SEQ ID NO.: 71),

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AGSFLAWL GSLLLGVLA -1
ADRERSIHDF CLVSKVVGRC RASMPRWYV VTDGSCQLFV YGGCDGNSNN 50
YLTKEECLKK CATVTENATG DLATSRNAAD SSVPSAPRRQ DSEDHSSDMF 100
NYEEYCTANA VTGPCRASFP RWYFDVERNS CNNFIYGGCR GNKNSYRSEE 150
ACMLRCFRQQ ENPPLPLGSK VVVLAGAVS 179
(SEQ ID NO.: 2),

	MLR AEADGVSRLL GSLLSGVLA	-1
	ADRERSIHDF CLVSKVVGRC RASMPRWYNN VTDGSCQLFV YGGCDGNSNN	50
	YLTKEECLKK CATVTENATG DLATSRNAAD SSVPSAPRRQ DSEDHSSDMF	100
5	NYEEYCTANA VTGPCRASFP RWYFDVERNS CNNFIYGGCR GNKNSYRSEE	150
	ACMLRCFRQQ ENPPLPLGSK VVVLAGLFVM VLILFLGASM VYLIRVARRN	200
	QERALRTVWS SGDDKEQLVK NTYVL	225
	(SEQ ID NO.: 45),	
10	MAQLCGL RRSRAFLALL GSLLSGVLA	-1
	ADRERSIHDF CLVSKVVGRC RASMPRWYNN VTDGSCQLFV YGGCDGNSNN	50
	YLTKEECLKK CATVTENATG DLATSRNAAD SSVPSAPRRQ DSEDHSSDMF	100
	NYEEYCTANA VTGPCRASFP RWYFDVERNS CNNFIYGGCR GNKNSYRSEE	150
	ACMLRCFRQQ ENPPLPLGSK VVVLAGLFVM VLILFLGASM VYLIRVARRN	200
15	QERALRTVWS FGD	213
	(SEQ ID NO.: 47),	
	ADRERSIHDF CLVSKVVGRC RASMPRWYNN VTDGSCQLFV YGGCDGNSNN	50
	YLTKEECLKK CATVTENATG DLATSRNAAD SSVPSAPRRQ DSEDHSSDMF	100
20	NYEEYCTANA VTGPCRASFP RWYFDVERNS CNNFIYGGCR GNKNSYRSEE	150
	ACMLRCFRQQ ENPPLPLGSK VVVLAGLFVM VLILFLGASM VYLIRVARRN	200
	QERALRTVWS FGD	213
	(SEQ ID NO.: 70);	
25	IHDF CLVSKVVGRC RASMPRWYNN VTDGSCQLFV YGGCDGNSNN	50
	YLTKEECLKK CATV	64
	(SEQ ID NO.: 4);	
	CLVSKVVGRC RASMPRWYNN VTDGSCQLFV YGGCDGNSNN	50
30	YLTKEECLKK C	61
	(SEQ ID NO.: 5);	
	YEEYCTANA VTGPCRASFP RWYFDVERNS CNNFIYGGCR GNKNSYRSEE	150
	ACMLRCFRQ	159
35	(SEQ ID NO.: 6);	
	CTANAVTGPC RASFPRWYFD VERNSCNNFI YGGCRGNKNS YRSEE	150
	ACMLRC	156

(SEQ ID NO.: 7);

1 IHDF CLVSKVVGRC RASMPRWYV VTDGSCQLFV YGGCDGNSNN 50
5 YLTKEECLKK CATVTENATG DLATSRNAAD SSVPSPRRQ DSEDHSSDMF 75
NYEEYCTANA VTGPCRASFP RWYFDVERNS CNNFIYGGCR GNKNSYRSEE 125
ACMLRCFRQ 159
(SEQ ID NO.: 3);

10 CLVSKVVGRC RASMPRWYV VTDGSCQLFV YGGCDGNSNN 50
YLTKEECLKK CATVTENATG DLATSRNAAD SSVPSPRRQ DSEDHSSDMF 100
NYEEYCTANA VTGPCRASFP RWYFDVERNS CNNFIYGGCR GNKNSYRSEE 150
ACMLRC 156
(SEQ ID NO.: 50);

15 ADRERSIHDF CLVSKVVGRC RASMPRWYV VTDGSCQLFV YGGCDGNSNN 25
YLTKEECLKK CATVTENATG DLATSRNAAD SSVPSPRRQ DSEDHSSDMF 75
NYEEYCTANA VTGPCRASFP RWYFDVERNS CNNFIYGGCR GNKNSYRSEE 125
ACMLRCFRQQ ENPPLPLGSK VVLAGAVS 179
(SEQ ID NO.: 1); and

20 ADRERSIHDF CLVSKVVGRC RASMPRWYV VTDGSCQLFV YGGCDGNSNN 50
YLTKEECLKK CATVTENATG DLATSRNAAD SSVPSPRRQ DS 92
(SEQ ID NO.: 8).

25 2. A protein as in claim 1, wherein said protein is glycosylated, or contains at least one intra-chain cysteine-cysteine disulfide bond, or is both glycosylated and contains at least one intra-chain cysteine-cysteine disulfide bond.

30 3. A pharmaceutical composition for inhibiting serine protease activity, comprising a protein of claim 1 plus a pharmaceutically acceptable carrier.

4. An isolated nucleic acid sequence which encodes for a protein of claim 1.

35 5. A self-replicating protein expression vector containing a nucleic acid sequence which encodes for and is capable of expressing a protein of claim 1.

6. A method for inhibiting serine protease activity comprising contacting serine protease with an effective amount of at least one protein of claim 1.

7. A method for treating a condition of brain edema, spinal cord edema, multiple sclerosis, ischemia, perioperative blood loss, sepsis, septic shock, fibrosis, disease associated with pathologic blood coagulation or clotting, polytrauma, stroke, 5 cerebral or subarachnoid hemorrhage, inflammation of the brain, inflammation of the spinal cord, cerebral infection, cerebral granulomatosis, spinal infection, spinal granulomatosis, open heart surgery, gastric cancer, cervical cancer, or prevention of metastasis comprising administering to a subject having such a condition and effective amount of the protein of claim 1 to a subject who requires treatment.

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8. The method of Claim 7 wherein said condition is brain edema, spinal cord edema, multiple sclerosis, ischemia, perioperative blood loss, sepsis, septic shock, fibrosis, disease associated with pathologic blood coagulation or clotting, stroke, cerebral or subarachnoid hemorrhage, inflammation of the brain, inflammation of the spinal cord, cerebral infection, cerebral granulomatosis, spinal infection, spinal granulomatosis, or open heart surgery.

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9. The method of Claim 7 wherein said condition is gastric cancer, cervical cancer, or prevention of metastasis.

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10. A method for the preparation of a medicament for the treatment of brain edema, spinal cord edema, multiple sclerosis, ischemia, perioperative blood loss, sepsis, septic shock, fibrosis, disease associated with pathologic blood coagulation or clotting, stroke, cerebral or subarachnoid hemorrhage, inflammation of the brain, inflammation of the spinal cord, cerebral infection, cerebral granulomatosis, spinal infection, spinal granulomatosis, open heart surgery, gastric cancer cervical cancer, or prevention of metastasis, comprising combining an effective amount of a protein 25 of claim 1 with a suitable pharmaceutical carrier or excipient.

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11. A method for preparing a protein of claim 1 using recombinant DNA technology.